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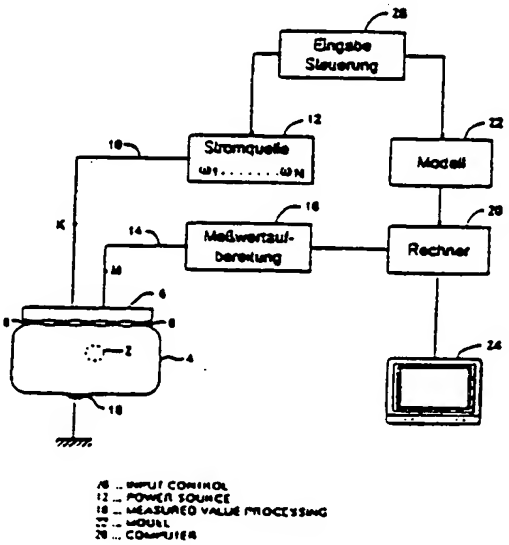
(54) Title: METHOD FOR LOCALISING AND IDENTIFYING SIGNAL ACTIVITIES OF AT LEAST ONE DELIMITED AREA IN A SECTION OF BIOLOGICAL TISSUE

(54) Bezeichnung: VERFAHREN ZUM LOKALISIEREN UND IDENTIFIZIEREN VON SIGNALAKTIVITÄTEN MINDESTENS EINES BEGRENZTEN RAUMGEBIETS IN EINEM BIOLOGISCHEN GEWEBEABSCHNITT

(57) Abstract

The invention relates to a method for localising and identifying signal sources of at least one delimited area (2) in a section (4) of biological tissue. According to said method electrical measurement data e_m (relating to potential or current) are measured (16) in several points (8) on a surface of the tissue section (4). These data arise on the tissue section (4) on the basis of a sequence of electrical currents of different frequencies produced by the injection of current into the tissue section and via the voltages between the points (8) on the surface of the tissue section (4). On the basis of the electrical data e_m (relative to potential or current) measured at the measurement points (8) the signal sources characterizing the area (2) are localised and identified by means of a method developed for spatio-temporal measurement values. Instead of the time-dependent measurement values the frequency-dependent potential values φ_m (in case of potential measurement) or current values j_m (in case of current measurement) measured at the measurement points (8) are used as input variables. The position and frequency-dependent activities of the signal sources are emitted as output variables.



(57) Zusammenfassung

Bei einem Verfahren zum Lokalisieren und Identifizieren von Signalquellen mindestens eines begrenzten Raumgebiets (2) in einem biologischen Gewebeabschnitt (4) werden elektrische Messdaten e_m (Potential- oder Stromdaten) an mehreren Orten (8) auf einer Oberfläche des Gewebeabschnittes (4) gemessen (16), die sich aufgrund einer Folge von durch Stromeinspeisungen in den Gewebeabschnitt bzw. durch Spannungen zwischen Oberflächenorten (8) des Gewebeabschnittes (4) erzeugten elektrischen Strömen mit unterschiedlicher Frequenz durch den Gewebeabschnitt (4) einstellen. Aus den an den Messorten (8) gemessenen elektrischen Daten (Potential- bzw. Stromdaten) e_m werden mit Hilfe eines für raum-zeitliche Messwerte entwickelten Verfahrens die das Raumgebiet (2) charakterisierenden Signalquellen lokalisiert und identifiziert. Dabei werden anstelle der zeitabhängigen Messwerte die an den Messorten (8) gemessenen frequenzabhängigen Potentialwerte φ_m (bei Potentialmessung) bzw. Stromwerte j_m (bei Strommessung) als Eingangsgrössen verwendet. Als Ausgangsgrossen werden Ort und frequenzabhängige Aktivitäten der Signalquellen ausgegeben.

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Description

Method for locating and identifying signal activities of at least one delimited region in a section of biological tissue

The invention relates to a method for locating and identifying signal activities of at least one delimited region in a section of biological tissue, which region has an electric impedance differing from the remaining section of tissue, the remaining section having an essentially spatially constant electric impedance.

A non-invasive determination of the electric impedance or the distribution of the electric impedance inside a section of biological tissue can be determined using methods of electric impedance tomography (EIT). The method is described, for example, in the article by B.H. Brown and D.C. Barber: "Electric impedance Tomography; the Construction and Application to Physiological Measurement of Electric impedance Images", which appeared in Medical Progress through Technology, Vol. 13, pages 69 to 75, which appeared in 1987 from Martinus Nijhoff Publishers, Boston. Via applied electrodes, alternating currents with frequencies in the range from 10 Hz to 50 kHz are impressed on the section of tissue to be examined, different narrower frequency ranges being used by various working groups. Sectional views of the distribution of conductivity or impedance are calculated in a tomographic reconstruction from the potentials arising in the process on the body surface. The reconstruction proceeds from a model of the section of tissue in which there is at first a homogeneous conductivity or impedance.

In order to set up accurate body models, it is customary to take values of the electric impedance from the literature, and these have been obtained ex vivo from preparations, or in one-off in-vivo examinations, preferably on the animal model.

The electric impedance, its relative magnitude in specific regions and its temporal change can be used for a medical diagnosis. Thus, for example, deviations of the electric impedance from normal values and/or normal distributions can be evaluated in tumor diagnosis and in connection with administering drugs and other therapeutic measures.

US-A 5 184 624, GB-A 2 273 987 and US-A 5 588 429 relate to methods of electric impedance tomography (EIT). This means: reconstruction methods are used to calculate impedance images from the measured data - here: potential values. These images are characterized in that they consist of a prescribed number of pixels which are allocated impedance values by the reconstruction method.

The external shape of a section of tissue can be determined using the reconstruction method described in US Patent 5,184,624. A plurality of electrodes are placed on the surface of the section of tissue. Electric currents are led into the section of tissue by one pair of electrodes in each case. The spacings of the electrodes from one another, and thus the external contour are determined from the potentials on the surface which arise therefrom. If the external contour of the section of tissue is known, a tomographic image of the internal structure can be constructed on the basis of the electric impedance tomography.

An improved method of data acquisition is proposed in GB-A 2 273 987. The data obtained are used, once again, to reconstruct a tomographic impedance image.

US-A 5 588 429 deals with methods for generating optimal current patterns which are injected into the body with the aid of the electrodes fitted on the body circumference, in order to obtain improved data for a reconstruction algorithm.

Accordingly, in the known methods of electric impedance tomography (EIT) images of the examination zone are reconstructed in which each pixel is assigned electrical conductivity values in accordance with the anatomical position.

In-vivo measurements of local tissue impedances with the aid of a needle electrode are described in the article by Y. Kinouchi et al [lacuna] "Fast in vivo Measurements of local tissue impedance using needle electrodes" in Medical & Biological Engineering & Computing, Vol. 35 (Sept. 1997), pages 486 to 492. These measurements are carried out using a plurality of frequencies in order to obtain the tissue-specific curves. These curves correspond to the known Cole-Cole plot.

In the article "Magnetic Imaging of Conductivity" which appeared in Proceedings of Annual International Conference of the IEEE Engineering in Medicine and Biology Society, Vol. 14, Paris 1992, pages 1717-1718, Seppo Ahlfors and Risto Ilmoniemi present a method which can be used to estimate a conductivity distribution inside an object. The object is injected via surface electrodes with a current whose magnetic field is measured and evaluated. By contrast with EIT, this method is named

magnetic impedance tomography (MIT). The impedance distribution is determined using locating methods such as have been developed in the field of biomagnetism. The approach in this case is that changes in conductivity change the magnetic field as if an equivalent current source were arranged at the location of the change in conductivity.

A method for reconstructing current dipoles in order to explain activities in the brain is described in the article by Mosher, Lewis and Leahy: "Multiple Dipole Modeling and Localization from Spatio-Temporal MEG Data" which appeared in IEEE Transactions on Biomedical Engineering, Vol. 39, No. 6, June 1992, pages 541-557. A model is used there to show how the determination of the parameters can be split up into determining time-invariant parameters and a linear determination, following thereupon, of the combined time-variant parameters. This method is a special case of the known MUltiple SIgnal Classification (MUSIC) method, in which the locations of a plurality of dipoles are found by means of a unidipole model by scanning all potential locations.

A method which can be used to locate and classify electrophysiological activities is described in the article by T. Elbert, M. Junghöfer, B. Scholz and S. Schneider entitled "The Separation of Overlapping Neuromagnetic Sources in First and Second Somatosensory Cortices", which appeared in Brain Topography, Volume 7, No. 4, 1995, pages 275-282. For this purpose, magnetic field values generated in a fashion resolved in space and time by the electrophysiological activities are measured and arranged in a spatio-temporal measured data matrix. Decomposing this matrix in terms of singularities permits the M-dimensional measured data space (M is the number of the sensors) to be decomposed into a signal space and a space orthogonal thereto. The dimension of the signal space is given by a number of

significant, linearly independent source activities resulting from the number of the numerically dominant singularities. Determining the location of the source activities consists in that at each location of the discretized examination zone a biophysical model is used as a basis for calculating theoretical magnetic field values as a consequence of a unit dipole placed there, and for establishing the extent to which a theoretical data vector formed thereby is an element of the signal space determined at the beginning. This is performed there by a system of linear equations which relates the basic vectors of the signal space and the theoretical magnetic field, already mentioned above, of the unit dipole by means of unknown coefficients and coefficients to be determined, and of the unit dipole moment to be determined. The measure of the extent to which the theoretical data vector belongs to the signal space is a target function which is the sum of the squares of the differences between the theoretical magnetic field values and the measured values which result from the calculated linear combination of signal space basic vectors. The locations of dipoles in the model are obtained as a result of the analysis of the target function. The time response of the dipoles results from a resolution of a system of equations in which the time dependence of the dipoles which is to be determined is simulated via the lead field of the measured values.

It is the object of the invention to specify a method for locating and identifying signal activities of at least one delimited region in a section of biological tissue.

The object is achieved by means of a method having the steps of:

- measuring (102) electric potential values ϕ_m or current values j_m at a plurality of measuring points $1 \leq m \leq M$ on a surface of the section (4) of tissue, which potential

values arise from a sequence of electric currents or electric voltages of different frequency ω_i, where $1 \leq i \leq N$, through the section of tissue, and/or which current values arise from a sequence of electric voltages of different frequency ω_i, where $1 \leq i \leq N$, between at least one reference electrode and at least one measuring electrode, which are located on the surface of the section of tissue,

- locating and identifying signal sources characterizing the region from the potential or current values, ϕ_m and j_m, respectively, measured at the measuring points, with the aid of a method developed for spatio-temporal measured values, the frequency-dependent potential values ϕ_m or current values j_m, measured at the measuring points, being used as input variables instead of the time-dependent measured values, and the output variables of location and frequency-dependent activity of the signal sources being output.

This method permits locating (determining the location) and characterizing (determining equivalent dipole moments) of spatially delimited conductivity zones which differ in conductivity from the surroundings. Tissue differentiations are thereby possible given a tissue-typical frequency dependence of a signal activity of the dipole. Methods developed in the field of biomagnetism, such as, for example, the methods of Mosher, Lewis and Leahy or of Elbert, Junghöfer, Scholz and Schneider mentioned at the beginning, are adapted as appropriate in this case.

The physical background of the method according to the invention will firstly be explained for the purpose of better understanding.

Owing to an electric field, electric polarization processes occur at interfaces of different conductivities and/or dielectric constants. These polarization processes have the effect that a spatially delimited zone - for example a sphere - is electrically polarized with a different conductivity than the surroundings, and the original electric field is changed by the additional polarization field.

Thus, the polarization field of the dielectric sphere in an infinite medium corresponds to the electric field of a punctiform dipole. A punctiform dipole is characterized, inter alia, by six parameters: the three spatial coordinates and the three components of the dipole moment vector.

The direction of the dipole moment vector is that of the original electric field. The absolute value of the dipole moment vector is proportional to the strength of the original electric field, to the difference between the dielectric constants of the sphere and its surroundings and, finally, is also proportional to the volume of the sphere.

In the case of spatially delimited inhomogeneities in conductivity and/or permittivity in a finite volumetric conductor, for example malignant or benign lesions in a region of the human body, polarization processes likewise occur in the region of the inhomogeneities. The inhomogeneities can therefore be described by electric dipoles, that is to say by six parameters. The concept of modeling differences in conductivity by means of dipoles is known in the literature. Reference is made here to the article by Ahlfors and Ilmoniemi mentioned at the beginning.

Reference may further be made to the fact that the electric conductivity is generally a complex variable (the term complex being used here in the mathematical sense) and is composed

of the direct-current conductivity and the generally complex, relative dielectric constants.

Because of relaxation processes, the dielectric constant depends on the frequency of the applied electric field. This frequency dependence is frequently represented as a Cole-Cole plot: the imaginary part of the dielectric constant is plotted against the real part of the dielectric constant with the frequency ω as parameter. The curve is a semicircle in the ideal case.

Since both the relaxation processes and the direct-current conductivity are tissue-specific, the electrical conductivity is a tissue-specific physical variable with regard to its values and its frequency dependence.

In particular, measurements show that both malignant and benign changes in tissue both among one another and with respect to the healthy surrounding tissue have different electrical conductivities.

The fact of different conductivities of the various types of tissue in the human body can be used for the purpose of biomedical imaging and other diagnostic methods.

An advantageous refinement is distinguished in that for the purpose of locating and identifying the signal sources, a model of the section of tissue is provided in the form of a vectorial lead field $\underline{\vec{L}}(\vec{r}_s)$ which is a function of the type of measured data (potential or current data) and potential signaling points $\vec{r}_s$ arranged in the volumetric conductor, and of model measuring points $\vec{r}_m$, corresponding to the measuring points, on the surface of the volumetric conductor, in that the measured

potential values are decomposed into signal values which belong as basic vectors $\underline{u}_1, \ldots, \underline{u}_n, \ldots \underline{u}_{N_{dom}}$ to a signal space U_{sig}, and into further values which belong to a space orthogonal to the signal space U_{sig}, in that for each potential signaling point $\vec{r}_s$ in the volumetric conductor a unit vector $\hat{d}$, associated with the lead field $\underline{L}(\vec{r}_s)$, of a signal activity, and coefficients c_n associated with the basic vectors $\underline{u}_n$ are determined such that for all model measuring points $\vec{r}_m$ there is the best possible correspondence between the model of the section of tissue and the signal values, in that a value of a target function F is determined (108) for each potential signaling point $\vec{r}_s$, which target function comprises deviations between the model and the signal values, in that each minimum of the target function is identified as a point $\vec{r}_1, \ldots, \vec{r}_s$ of a signal activity $\vec{d}_1, \ldots, \vec{d}_s$, and in that from the electrical measured data $\underline{\varphi}(\omega) = (\varphi_1(\omega), \ldots, \varphi_M(\omega))^T$, which can be either potential values ϕ_m or current values j_m, depending on the electronic system for measured data acquisition connected downstream of electrodes, and the lead fields $\underline{L}(\vec{r}_1), \ldots, \underline{L}(\vec{r}_s)$, which depend on the type of measured value, determined by the points $\vec{r}_1, \ldots, \vec{r}_s$ of the signal activities $\vec{d}_1, \ldots, \vec{d}_s$ are used to determine a frequency dependence $\vec{d}_1(\omega), \ldots, \vec{d}_1(\omega)$ of each signal activity. This approach has the advantage that by comparison with the tomographic reconstruction of conductivity fewer parameters need be determined for locating and characterizing regions with a conductivity differing from the surroundings.

A further advantageous refinement is distinguished in that the basic vectors $\underline{u}_n$ in the signal space U_{sig} are determined via a singularity decomposition of the measured electric data (measured potential or current values) present as a matrix **E**

$$E = \begin{pmatrix} e_1(\omega_1) \cdots e_1(\omega_N) \\ \vdots \qquad\qquad \vdots \\ e_M(\omega_1) \cdots e_M(\omega_N) \end{pmatrix}$$

in accordance with

$$E = USV^T$$

U representing a matrix depending only on the indices of the measuring points, S representing a diagonal singularity matrix, and V representing a matrix dependent only on frequency indices, and in that only the column vectors $\underline{u}_n$, where $1 \leq n \leq N_{dom}$, of the matrix U which are associated with numerically dominant singularities are further processed as basic vectors, N_{dom} signifying the index of the last numerically dominant singularity. The singularity decomposition per se is a standard mathematical method for analyzing non-square matrices. Singularities are generalizations of the eigenvalues in the case of square matrices.

A further advantageous refinement is distinguished in that the unit vector associated with the lead field, and the coefficients associated with the basic vectors are determined as solutions of a system of equations for the purpose of the Gaussian method of root-mean-square values

$$\sum_{n=1}^{N_{dom}} c_n \left(\vec{r}_s\right) \underline{u}_n \equiv \vec{\underline{L}} \left(\vec{r}_s\right) \cdot \hat{d}$$

n_{dom} being the number of the numerically dominant singularities. The system of equations expresses the theoretically calculated magnetic field, as given on the right-hand side of the equation, through a linear combination of basic vectors of the signal space as specified on the left-hand side of the equation. If there exists for the coefficients c_n and for the unit dipole moment at the point considered a solution differing from zero, this means that at this point the data vector of the model magnetic field is situated entirely or partially in the signal space. The measure of this membership is the value of the target function. Although it could also be established using the projection method specified by Mosher, Lewis and Leahy with regard to biomagnetism whether the model data vector is situated in the signal space or not, the foregoing method offers the advantage that the system of equations can be solved explicitly and therefore requires less computer time.

In a further advantageous refinement, the target function is determined in accordance with the relationship

$$F = \left\| \sum_{n=1}^{N_{dom}} c_n \left(\vec{r}_s\right) \underline{u}_n - \underline{\vec{L}} \left(\vec{r}_s\right) \cdot \hat{d} \right\|^2$$

and the minima of the target function are determined at the points $\vec{r}_1, \ldots, \vec{r}_s$ as points of actual signal activity.

A further advantageous refinement is distinguished in that the frequency dependence of the signal activities $\underline{d}=(\vec{d}_1, \ldots, \vec{d}_s)$ are determined at the points $\vec{r}_1, \ldots, \vec{r}_s$ in accordance with the relationship

$$\underline{d}(\omega) = (\Lambda^T \Lambda)^{-1} \Lambda^T \underline{e}(\omega)$$

in which case

$\Lambda = \left(\underline{\bar{L}}(\bar{r}_1), \ldots, \underline{\bar{L}}(\bar{r}_s)\right)$ and

$\underline{e}(\omega) = (e_1(\omega), \ldots, e_M(\omega))^T$.

The invention is explained below with the aid of five figures, in which:

Figure 1 shows an overview of the essential components of a device for locating and identifying signal activities,

Figure 2 shows the essential method steps for locating and identifying signal activities,

Figure 3 shows a field-strength distribution calculated in a simulation given homogeneous conductivity,

Figure 4 shows a field-strength distribution calculated in a simulation given a subcuboid of different conductivity, and

Figure 5 shows the differential field-strength distribution of Figures 3 and 4.

The overview in Figure 1 shows a measuring and evaluation arrangement, it being possible to locate and identify signal activities of a delimited region 2 in a section 4 of biological tissue. It is assumed in this case that the region 2 has an electric impedance differing from the remaining section 4 of tissue, the remaining section 4 of tissue having an electric impedance which is essentially spatially constant. These assumptions are adequately fulfilled when the section 4 of biological tissue is a female breast and the delimited region 2 is a tumor.

The measuring arrangement includes an applicator 6 with a multiplicity of electrodes 8 which are arranged distributed in space and are brought into contact with the surface of the section 4 of tissue. For reasons of clarity, Figure 1 illustrates only five electrodes 8, although actually there should, for example, be M = 256 electrodes 8 arranged on a surface of 9×9 cm^2.

The electrodes 8 are connected, on the one hand, to a current source or a voltage source 12 via connecting lines 10 and, on the other hand, to a measured-value conditioner 16 via connecting lines 14. Arranged on the side of the section 4 of tissue opposite the applicator 6 is a counterelectrode 18 which is likewise connected to the current source 12 in the case of potential measurements, or to the voltage source 12 in the case of current measurements and the measured-value conditioner 16. It is also possible to configure a part of the applicator 6 as counterelectrode. In the case of potential measurements, alternating currents, and in the case of current measurements alternating voltages are fed with the aid of the current or voltage source 12 to the section 4 of biological tissue via a number of K electrodes 8, where $1 \leq K \leq M$, in order to generate there a spatial current distribution. The currents fed in, or the voltages applied, externally electrically polarize delimited regions 2, which have an impedance different from the surrounding tissue 4, in such a way that the now polarized regions 2 can be regarded approximately as focal bioelectric signal sources.

The polarization of such a region 2, and the electric field generated thereby are shown in Figures 3, 4 and with the aid of simulation data. The simulated section 4 of tissue may be a 120×120×56 mm^3 cuboid consisting of fat tissue. The measuring electrode system 8, of size 62×62 mm^2, is arranged centered on the top face, of size 120×120 mm^2, of the cuboid. The reference

electrode 18 is of size 30×30 mm^2 and fitted in a centered fashion on the bottom face. The region 2 is a small subcuboid, of size 6×6×6 mm^3 at a depth of 16 mm (the z-coordinate of the top edge of the subcuboid is 16 mm; note: the positive z-axis is directed downward). It is assumed that the subcuboid consists of cancerous tissue. Figure 3 shows the distribution of the strength of the electric field in a vertical cuboid plane in the case of homogeneous conductivity. This plane intersects the region 2 in the case of the inhomogeneous cuboid (cuboid with subcuboid of different conductivity). The electric field is deformed by the region 2, see Figure 4. Figure 5 shows [lacuna] differential field of Figure 3 and Figure 4. The dipolar-like electric polarization field excited from outside by the spatially limited inhomogeneity in conductivity may be seen.

The respective signal strength is a function of the magnitude and of the frequency-dependent complex conductivity of the region 2 considered. Locating and identifying spatially delimited regions 2 amounts to finding and determining the strength of such bioelectric signal sources by measuring the potentials, generated by the currents fed in, on the surface of the section 4 of tissue at M electrode locations, or measuring the currents, generated in the section 4 of tissue by the applied voltages, at the M electrode locations, and feeding them to an evaluation unit. Since the frequency dependence of the impedance in the delimited regions 2 constitutes an important variable for characterizing the corresponding tissue, currents with N different frequencies which are, for example, in the region from 10 to 50 kHz, can be generated by the current source and fed to the section 4 of tissue.

The measured-value conditioner 16 comprises, for example, measuring amplifier, filter and analogue-to-digital converter. The measured-value conditioner 16 is

connected to one or more data inputs of an electronic computer 20. In addition to the measured values, a model 22 of the section 4 of tissue is made available to the computer, and the abovementioned bioelectric signal sources are located and identified with its aid, as is further described below. The result, for example in the form of a graphical illustration of the section of tissue in which the location of the signal sources, and thus the regions 2, are marked, and a variable characterizing the signal activity as a function of the current frequencies is illustrated, is performed via a monitor 24. Since the model 22 is a function of a current pattern generated in the section 4 of tissue or at the feed location, a master input and controller 26 is provided which presets the number and the location of the feed electrodes 8 and of the voltage electrodes 8, the value of the current frequency or voltage frequency and the model.

As already mentioned above, for the purpose of locating and identifying the method utilizes the fact that sufficiently delimited regions 2 which have a different impedance from the surrounding region 4 are electrically polarized by the externally fed alternating currents or the externally applied AC voltages. The respective signal strength depends on the magnitude and on the frequency-dependent complex conductivity of the considered region of inhomogeneity of the impedance. Detecting changes in impedance such as represent tumors, for example, therefore amounts to finding and determining the strength of the above-named bioelectric signal sources.

In order also to be able to locate a plurality of focal signal sources activated by current or voltage frequencies, the measured potential values are subjected to a processing and evaluation method as described similarly in the publication, already quoted at the beginning, by Elbert et al.

for locating temporally overlapping multifocal bioelectric activities. This multi-dipole locating method developed originally for spatio-temporal measured data is applied here to spatio-frequency measured data. The evaluation is performed via an appropriate program on the computer 20. Input data are, firstly, the elements, dependent on the indices m of the current or voltage frequencies, of the one measured value matrix E (method step 102). The measured value matrix E can accordingly be specified in the following form:

$$E = \begin{pmatrix} e_1(\omega_1) \cdots e_1(\omega_N) \\ \vdots \quad\quad \vdots \\ e_M(\omega_1) \cdots e_M(\omega_N) \end{pmatrix}$$

Set up as a further input variable (method step 103) is a vectorial lead field $\underline{\vec{L}}(\vec{r})$ which corresponds to the volumetric conductor model of the section of tissue to be examined and which contains a description of electrodes 8 with regard to their locations and nature such as, for example, extended or punctiform. The vectorial lead field is a function of the type of measured values (potential or current values), of the measuring point and of the potential signaling point $\vec{r}_s$, and may be represented as follows using vector notation:

$$\underline{\vec{L}}(\vec{r}_s) = \left(\underline{L}_x(\vec{r}_s), \underline{L}_y(\vec{r}_s), \underline{L}_z(\vec{r}_s)\right)$$

where $\underline{L}_x = \begin{pmatrix} L_{x1} \\ \vdots \\ L_{xm} \\ \vdots \\ L_{xM} \end{pmatrix}$, $\underline{L}_y = \begin{pmatrix} L_{y1} \\ \vdots \\ L_{ym} \\ \vdots \\ L_{yM} \end{pmatrix}$, $\underline{L}_z = \begin{pmatrix} L_{z1} \\ \vdots \\ L_{zm} \\ \vdots \\ L_{zM} \end{pmatrix}$

in each case represents an M-dimensional field in the M-dimensional data space, with $1 \leq m \leq M$ as indices of the corresponding measuring points in the model;

The underscore therefore denotes the M-dimensional combination of the lead fields relating to the M electrode locations.

In a first processing step 104 of the program, the data matrix E is subjected to a singularity decomposition in accordance with

$$\boldsymbol{E = USV^T}$$

The singularity decomposition yields an M × M matrix U, which depends only on spatial indices of the electrodes, a diagonal singularity matrix S and a matrix V which depends only on frequency indices.

The singularity decomposition supplies the numerically dominant singularities and the column vectors associated therewith

$$\underline{u}_1, \ldots, \underline{u}_n, \ldots, \underline{u}_{N_{dom}}$$

The underscore once again signifies the M-dimensional combination of the column vectors associated with the M electrode locations. Numerically dominant means that the singularities $S_1, \ldots, S_{N_{dom}}$ are numerically greater than the remaining singularities.

In a further processing step 106, the following system of equations is solved:

$$\sum_{n=1}^{N_{dom}} c_n \left(\vec{r}_s\right) \underline{u}_n \equiv \vec{\underline{L}} \left(\vec{r}_s\right) \cdot \vec{d}$$

for each potential signaling point in the volumetric conductor model in accordance with the Gaussian method of root-mean-square values.

Here, the coefficients c_n and two independent components of a frequency-independent three-dimensional unit vector $\hat{d}$ are the unknowns to be calculated.

In the next processing step 108, a value of a target function F is calculated for each potential signaling point in the volumetric conductor. In this case, the relationship

$$F = \left\| \sum_{n=1}^{N_{dop}} c_n \left(\vec{r}_s\right) \underline{u}_n - \underline{\vec{L}} \left(\vec{r}_s\right) \cdot \hat{d} \right\|^2$$

$$= \sum_{m=1}^{M} \left[\sum_{n=1}^{N_{dop}} c_n \left(\vec{r}_s\right) \underline{u}_m \equiv \overline{L_m} \left(\vec{r}_s\right) \cdot \hat{d} \right]^2$$

is analyzed as target function F.

An extreme value analysis of the target function supplies S ($S \geq 0$) minima in accordance with the number of the regions of different electric impedance (processing step 110). The minima of the target function are identified with the points $\vec{r}_1, \ldots, \vec{r}_S$ of the signal sources and output, for example, on the monitor 24, their activities $\vec{d}_1(\omega), \ldots, \vec{d}_S(\omega)$, which depend on the frequency, still requiring to be determined.

The signal activities $\vec{d}_1(\omega), \ldots, \vec{d}_S(\omega)$ can be determined from a generalized inversion of the relationship between the M measured values $\underline{e}(\omega) = (e_1(\omega), \ldots, e_M(\omega))^T$ for a given current or voltage frequency and the signal activities $\underline{d}(\omega) = (\vec{d}_1(\omega), \ldots, \vec{d}_S(\omega))$, combined into a vector, as a function of the current or voltage frequency. The frequency res-

ponse of the signal activities is associated with the tissue-specific complex conductivity. It holds that

$$\underline{e}(\omega) = \Lambda \underline{d}(\omega),$$

[lacuna] M × 3S being a matrix which can be set up as follows

$$\Lambda = \left(\underline{L}_x(\vec{r}_1), \underline{L}_y(\vec{r}_1), \underline{L}_z(\vec{r}_1), \cdots, \underline{L}_x(\vec{r}_S), \underline{L}_y(\vec{r}_S), \underline{L}_z(\vec{r}_S)\right)$$

From the generalized inversion of this relationship, it is then possible in processing step 112 to determine the signal activities from the measured potential or current values:

$$\underline{d}(\omega) = (\Lambda^T \Lambda)^{-1} \Lambda^T \underline{e}(\omega)$$

The frequency-dependent signal activities are likewise output on the monitor in a suitable form, for example as a diagram.

Knowledge of the signal activity as a function of the current or voltage frequency permits a tissue characterization which is then determined by comparing the measured signal activity and typical signal activities of the individual tissue classes.

Patent claims

1. A method for locating and identifying signal sources of at least one delimited region (2) in a section (4) of biological tissue, which region (2) has an electric impedance differing from the remaining section (4) of tissue, the remaining section (4) of tissue having an essentially spatially constant electric impedance, having the steps of:

- measuring (102) electric potential values ϕ_m or current values j_m at a plurality of measuring points $1 \leq m \leq M$ on a surface of the section (4) of tissue, which potential values arise from a sequence of electric currents or electric voltages of different frequency ω_i, where $1 \leq i \leq N$, through the section of tissue, and/or which current values arise from a sequence of electric voltages of different frequency ω_i, where $1 \leq i \leq N$, between at least one reference electrode and at least one measuring electrode, which are located on the surface of the section of tissue,
- locating and identifying signal sources characterizing the region from the potential or current values, ϕ_m and j_m, respectively, measured at the measuring points, with the aid of a method developed for spatio-temporal measured values, the frequency-dependent potential values ϕ_m or current values j_m, measured at the measuring points, being used as input variables instead of the time-dependent measured values, and the output variables of location and frequency-dependent activity of the signal sources being output.

2. The method as claimed in claim 1,, characterized in that provided for locating and identifying the signal sources is a vectorial lead field (103) which corresponds to the model of the section (4) of tissue and the type of measurement (potential or current measurement) and is a function of potential signaling points $\vec{r}_s$ arranged in the volumetric conductor, and of model measuring points $\vec{r}_m$, corresponding to the measuring points, on the surface of the volumetric conductor, in that the electric measured values (potential or current values) are decomposed (104) into signal values which belong as basic vectors $\underline{u}_1, \ldots, \underline{u}_n, \ldots, \underline{u}_{N_{dom}}$ to a signal space U_{sig}, and into further values which belong to a space U_{sig} orthogonal to the signal space U_{sig}, in that for each potential signaling point $\vec{r}_s$ in the volumetric conductor a unit vector $\hat{d}$, associated with the lead field $\underline{\vec{L}}(\vec{r}_s)$, of a signal activity, and coefficients c_n associated with the basic vectors $\underline{u}_n$ are determined such that for all model measuring points $\vec{r}_m$ there is (106) the best possible correspondence between the model of the section of tissue and the signal values, in that a value of a target function F is determined (108) for each potential signaling point $\vec{r}_s$, which target function comprises deviations between the model and the signal values, in that each minimum of the target function is identified as a point $\vec{r}_1, \ldots, \vec{r}_s$ of a signal activity $\vec{d}_1, \ldots, \vec{d}_s$, and in that the measured potential values $\underline{\Phi}(\omega) = (\phi_1(\omega), \ldots, \phi_M(\omega))$ and the lead fields $L(\vec{r}_1), \ldots L(\vec{r}_S)$ determined by the points $\vec{r}_1, \ldots, \vec{r}_s$ of the signal activities $\vec{d}_1, \ldots, \vec{d}_s$

are used to determine (112) a frequency dependence $\overline{d_1}(\omega), \ldots, \overline{d_s}(\omega)$ of each signal activity.

3. The method as claimed in claim 2, characterized in that the basic vectors $\underline{u}_n$ in the signal space U_{sig} are determined (104) via a singularity decomposition of the measured electric data (potential or current values) present in matrix form in accordance with

$$\boldsymbol{E = USV^i}$$

U representing a matrix depending only on the indices of the measuring points, S representing a diagonal singularity matrix, and V representing a matrix dependent only on frequency indices, and in that only the column vectors $\underline{u}_n$, where $1 \leq n \leq N_{dom}$, of the matrix U which are associated with numerically dominant singularities are further processed as basic vectors of the signal space $\mathbf{U_{sig}}$, N_{dom} signifying the index of the last numerically dominant singularity.

4. The method as claimed in claim 3, characterized in that the unit vector associated with the lead field, and the coefficients associated with the basic vectors are determined (106) as solutions of a system of equations for the purpose of the Gaussian method of root-mean-square values

$$\sum_{n=1}^{N_{dom}} c_n \left(\overline{r_s}\right) \underline{u}_n \equiv \underline{\bar{L}} \left(\overline{r_s}\right) \cdot \hat{d}$$

n_{dom} being the number of the numerically dominant singularities.

5. The method as claimed in claim 4, characterized in that the target function is determined in accordance with the relationship

$$F = \left\| \sum_{n=1}^{N_{dop}} c_n \left(\vec{r}_s\right) \underline{u}_n - \underline{\vec{L}} \left(\vec{r}_s\right) \cdot \hat{\vec{d}} \right\|^2$$

and in that the minima of the target function are determined (108) at the points $\vec{r}_1, \ldots, \vec{r}_s$ as points of actual signal activity.

6. The method as claimed in claim 5, characterized in that the frequency dependence of the signal activities $\underline{d}=(\vec{d}_1, \ldots, \vec{d}_s)$ [lacuna] target function are determined (112) at the points $\vec{r}_1, \ldots, \vec{r}_s$ in accordance with the relationship

$$\underline{d}(\omega) = (\Lambda^T \Lambda)^{-1} \Lambda^T \underline{e}(\omega)$$

in which case

$\Lambda = \left(\underline{\vec{L}}(\vec{r}_1), \ldots, \underline{\vec{L}}(\vec{r}_s)\right)$ and

$\underline{e}(\omega) = (e_1(\omega), \ldots, e_M(\omega))^T$.

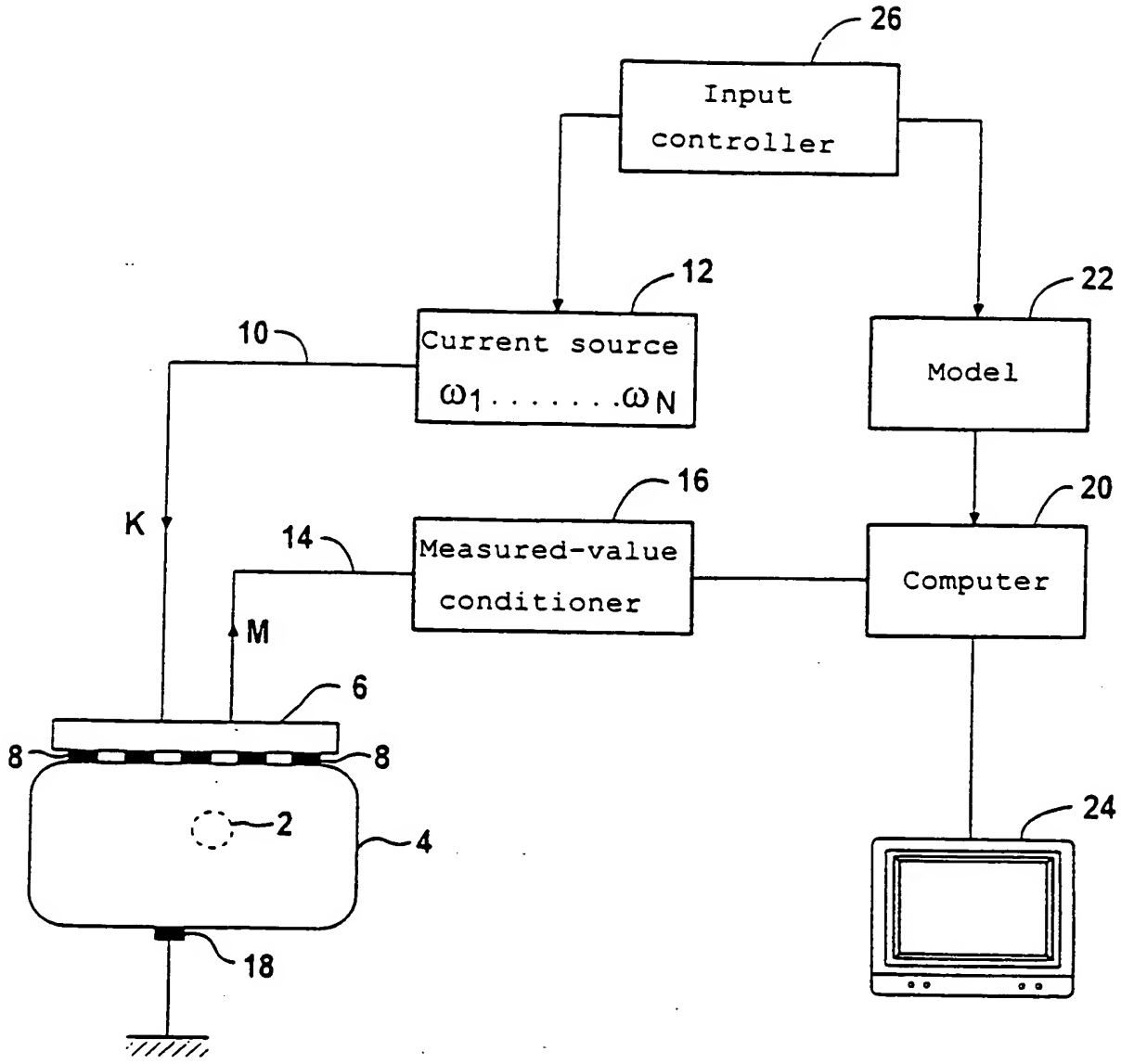
26
Input controller
12
22
10
Current source
$\omega_1 \ldots\ldots \omega_N$
Model
16
20
K
14
Measured-value conditioner
Computer
M
6
8
8
2
4
24
18

FIG 1

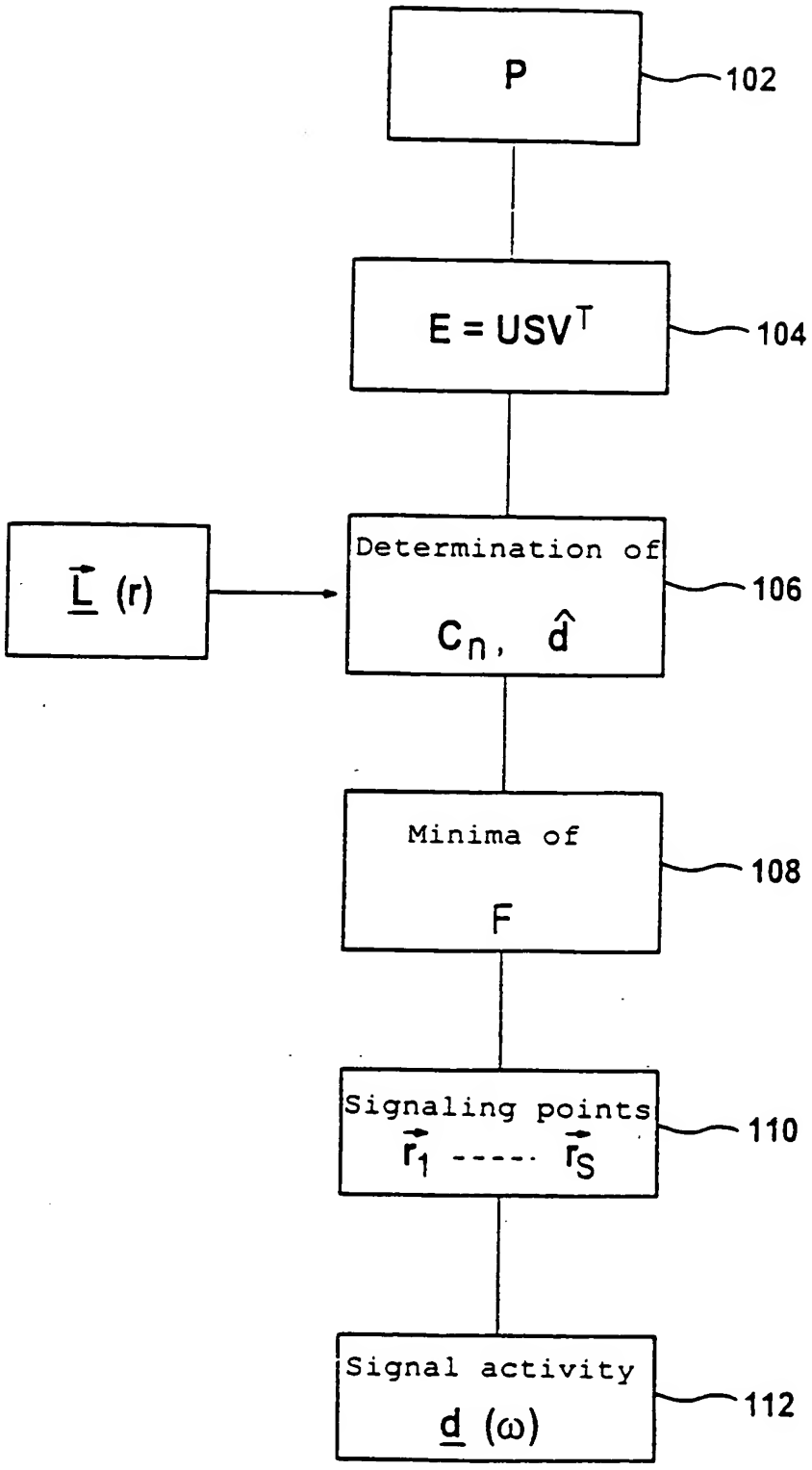
P
102
E = USV^T
104
L (r)
Determination of
C_n, d̂
106
Minima of
F
108
Signaling points
r_1 ----- r_S
110
Signal activity
d (ω)
112

FIG 2

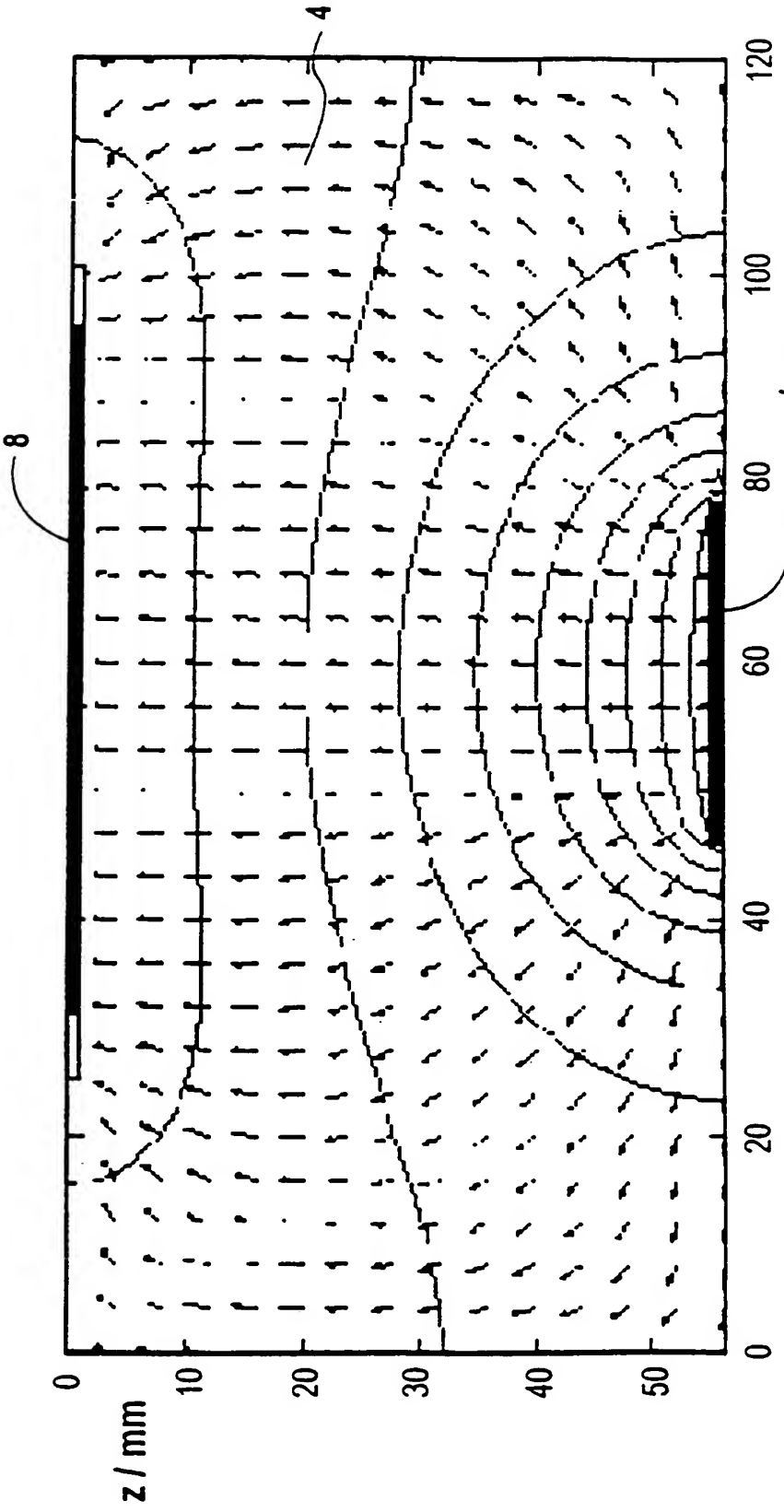

FIG 3

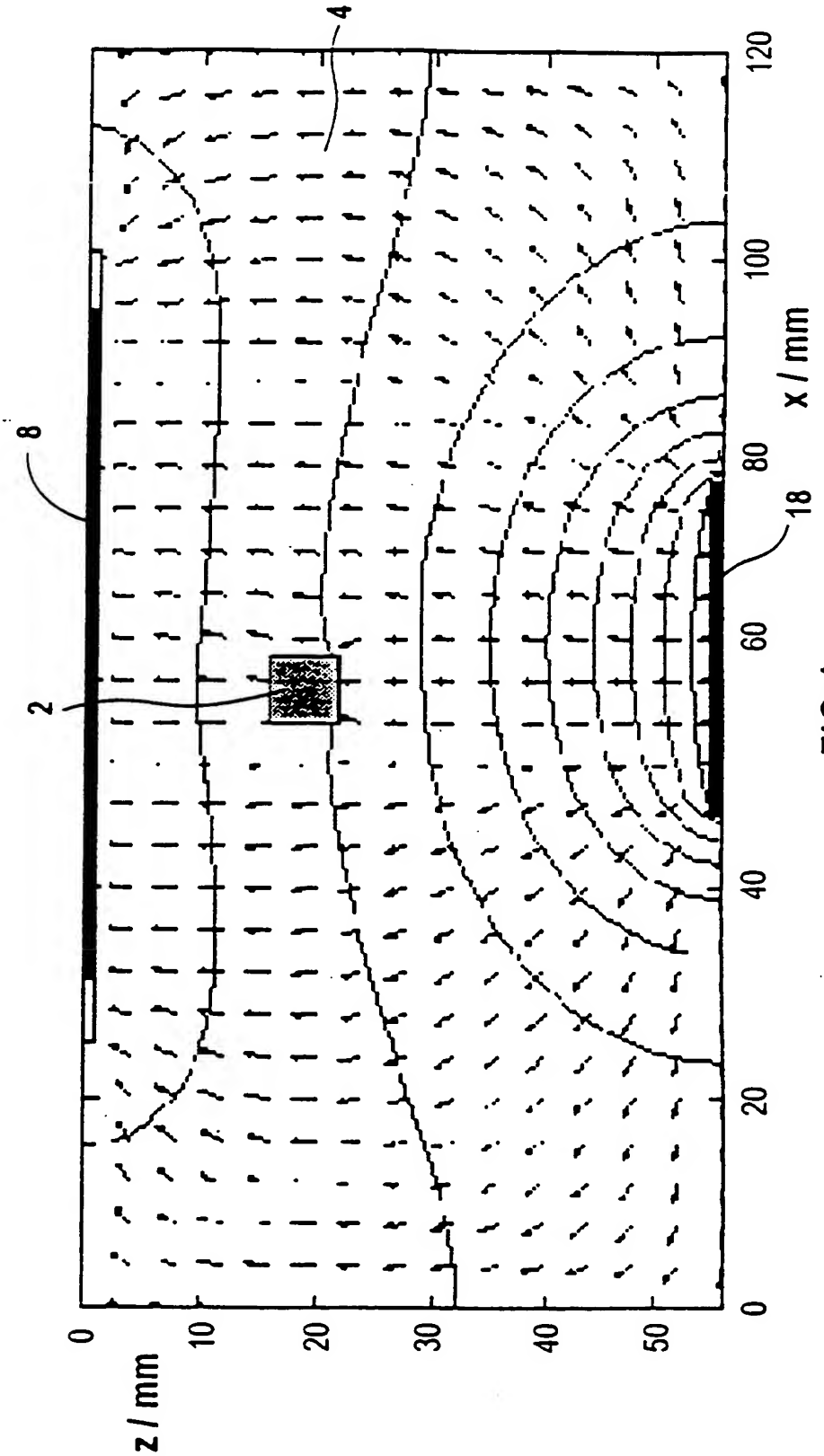

FIG 4

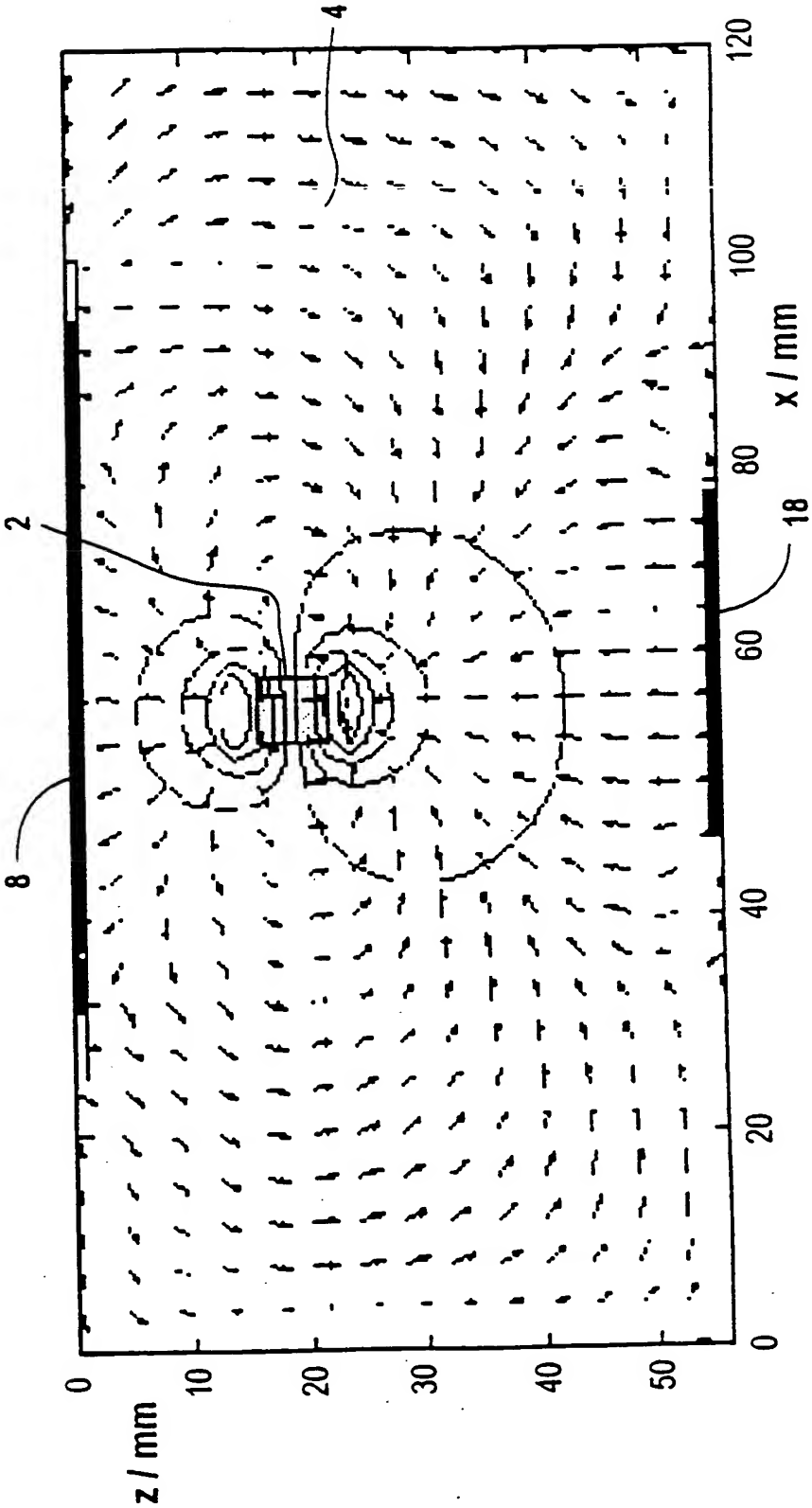

FIG 5